Remarks

Of the originally filed claims 1-35, claims 1-11, 14-21 and 23, drawn to DNA, were elected, with traverse, in response to a restriction requirement. In the Office Action mailed January 2, 2002, the Examiner indicated that only claims 3, 4, 6-10, 14, 16-21 and 23 read on the elected invention, however the remaining claims (i.e., claims 1, 2, 5, 11 and 15) were not withdrawn from examination (see below for a more detailed discussion of claim status).

Accordingly, claims 8, 9 and 16 having been canceled, claims 3-6, 10, 11, 14, 18 and 23 having been amended, and claims 36 and 37 having been added, the pending claims are claims 1-7, 10-15 and 17-35. Of the pending claims, claims 12, 13, 22 and 24-35 have been withdrawn from consideration by the Examiner, such that claims 1-7, 10, 11, 14, 15, 17-21 and 23 are presently under examination.

Support for the amendment of claim 3 reciting an antigenic portion of an i-antigen polypeptide comprising *at least about 60 amino acids* is found in the specification at, for example, page 20, line 10. Support for the further amendment of claim 3 and for the amendment to claim 11 reciting an immune response in fish against *I. multifiliis* is found, for example, in the specification at page 19, lines 16-18.

Support for the amendment of claim 4 reciting a polynucleotide fragment having a nucleotide sequence that encodes at least one terminal portion of an i-antigen polypeptide having amino acid sequence SEQ ID NO:7, said terminal portion comprising *at least about 10 amino acids*, is found in the specification at, for example, page 20, line 10.

Claims 5 is rewritten to recite a polynucleotide fragment having a nucleic acid sequence that encodes SEQ ID NO:7 rather than specific nucleotide sequences; specific nucleotide sequences that encode SEQ ID NO:7 are now recited in new claim 36 which depends from claim 5. Likewise claims 11 and 14 are amended to recite additional nucleotide sequences that encode amino acid sequence SEQ ID NO:7. In this regard, the Examiner is requested to note that SEQ ID NO:7 is the amino acid sequence of the 55 kDa i-antigen protein isolated from *I. multifiliis*

(see Fig. 3a). The following *nucleotide sequences* encode the protein represented by SEQ ID NO:7:

SEQ ID NO:3 (coextensive with the coding region; see specification at page 15, lines 23-24 and Fig. 3b)

SEQ ID NO:5 (preferred codon usage; see specification at page 15, lines 23-24, and page 16, line 28)

SEQ ID NO:44 (coding region includes nucleotides 1-1404; see Fig. 2a), and

SEQ ID NO:102 (coding region includes nucleotides 1-1404; see Fig. 2b).

Claim 6 is amended to delete the recitation of "organism."

Claims 8 and 9 are canceled, without prejudice.

Claims 6, 10, 14 and 23 are amended to change a dependency in view of the restriction election and the addition of claim 36. Claim 16 is canceled, without prejudice, as being redundant since its subject matter is now recited in claim 14.

Examiner Interview Summary

The Office is thanked for the personal interview April 17, 2002, extended to Applicants' Representative Victoria A. Sandberg by Examiners Fields, Navarro, Smith and Hutzell. All claims were discussed.

Applicants' Representatives pointed out numerous inconsistencies in the Office Action and Office Action Summary, including a failure to act on, either by rejecting or explicitly allowing, a number of the claims presently under examination. Applicants requested that the next action, if anything other than a Notice of Allowance, be made nonfinal. Although it is not explicitly documented in the Interview Summary provided by the Examiner at the time of the interview, Applicants' Representative recall that this request was considered reasonable and was agreed to by the parties to the interview.

Applicants asserted that claims 5 and 11 read on the elected invention, and should therefore have been examined. Applicants agreed to provide support for that assertion in this response by explaining the relationship between and among the various nucleic acid sequences.

In response to the rejection under 35 U.S.C. §102(b), Applicants' Representative pointed out differences between the claimed invention and the nucleotide and protein sequences taught in Clark et al. by comparing Fig. 1 of Clark et al. to Figs. 1 and 3(b) of the above-identified patent application. Amino acid sequences SEQ ID NO:7 (a 55 kDa i-antigen) and SEQ ID NO:6 (a 48 kD antigen) were both distinguished from the teachings of Clark et al.

The rejections under 35 U.S.C. §112, second paragraph, were also discussed. Applicants pointed out that most of the terms objected to by the Examiner were defined in the specification and offered to point out the relevant sections of the specification in this response.

Restriction Requirement and Scope of Examination

The invention of Group 1 (claims 1-11, 14-21 and 23) was elected with traverse in Applicants' Response to the Restriction Requirement mailed July 3, 2001. The claims were further restricted under MPEP 803.04. In response thereto Applicants elected with traverse *nucleotide sequences* encoding at least a portion of *amino acid sequence* SEQ ID NO:7, and *nucleotide sequences* encoding at least a portion of a 55 kDa-i-antigen protein.

In the Office Action mailed January 2, 2002, the Examiner indicated that the claims reading on the elected invention are claims 4, 6-10, 14, 16-21 and 23. Applicants respectfully submit that this list should include claims 5 and 11.

Claim 5 is directed to a nucleic acid molecule comprising SEQ ID NO:3 or SEQ ID NO:5. Both of these nucleotide sequences encode the protein represented by SEQ ID NO:7 and thus should be included in the elected invention.

Claim 11 is directed to a nucleic acid molecule comprising a polynucleotide fragment that hybridizes to at least a portion of the complement of at least one of SEQ ID NO:1 or SEQ ID NO:3, with certain additional conditions. The nucleotide sequence SEQ ID NO:3 encodes the protein represented by SEQ ID NO:7; thus this claim should also be included in the elected invention.

It is thus respectfully requested that claims 5 and 11 be examined with 4, 6-10, 14, 16-21 and 23, and that the next Office Action, if it does not communicate allowance of the examined claims, be made non-final in order to allow the Applicants a full and fair opportunity to address any rejections of these newly examined claims.

Status of Claims

Applicants have several questions concerning the information represented in items 4-7 of the "Disposition of the Claims," page 1 of the Office Action mailed January 2, 2002.

Item 4 indicates that claims 1-40 are pending. Applicants' records indicates that only claims 1-35 are pending. Thus item 4 incorrectly indicates that claims 1-40 are pending.

Item 6 indicates that claims 1-11, 14-21 and 23 are rejected, even though only claims 4, 6-10, 14, 16-21 and 23 were actually examined. In other words, although claims 1, 2, 5, 11 and 15 were not examined (presumably because, in the Examiner's view, they did not read on the elected invention), they were not actually removed from examination and thus appear still to be subject to examination.

Furthermore, the Office Action mailed January 2, 2002, shows no rejections of record for claims 1, 2, 5, 11, 14, 15, 17, 19-21 and 23. It is noted that a rejection of any of these claims in the next office action would be a new grounds of rejection. Thus, an office action that includes a rejection of these claims can not be a final office action. Item 5 currently indicates that no claims are allowed. However, a review of the Office Action indicates that claims 1, 2, 5, 11, 14, 15, 17, 19- 21 and 23 are neither withdrawn from consideration hor have they been rejected, and as such appear to be allowable.

Clarification and correction of these items is kindly requested.

The 35 U.S.C. §102(b) Rejection

The Examiner rejected claims 3-4, 6-10, 16, and 18 under 35 U.S.C. §102(b) as being anticipated by Clark et al. (PNAS, 89:6363-6367 (1992)). This rejection is respectfully traversed.

Claim 3, as amended, is drawn to a nucleic acid molecule comprising a polynucleotide fragment having a nucleotide sequence that encodes an antigenic portion of an i-antigen polypeptide having amino acid sequence SEQ ID NO:7. The antigenic portion comprises at least about 60 amino acids and is capable of inducing an immune response in a fish against *I. multifiliis*.

Claim 4, as amended, is drawn to a nucleic acid molecule comprising a polynucleotide fragment having a nucleotide sequence that encodes at least one terminal portion of an i-antigen polypeptide having amino acid sequence SEQ ID NO:7. The terminal portion comprises at least about 10 amino acids.

Claim 5 as amended, which was not examined, is drawn to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:44 and SEQ ID NO:102. Each of these nucleic acid sequences encodes SEQ ID NO:7.

Claims 6, 7 and 10 depend, directly or indirectly, from claims 3, 4 or 5.

Claims 8, 9 and 16 are canceled, without prejudice, rendering the rejection moot with respect to those claims.

Claim 18 depends from a claim (namely, claim 14) which is neither withdrawn from consideration nor rejected. As a result the rejection of claim 18 under 35 U.S.C. §102(b) appears to be improper because the claim from which it depends is ostensibly free of the prior art.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP § 2131.

Clark et al. teach the polynucleotide sequence of a cDNA encoding a portion of a *48 kDa i-antigen* from an *I. multifiliis G1 isolate*, serotype A. This nucleotide sequence represents a portion of nonelected SEQ ID NO:6 (specifically, amino acids 22 through 409 as shown in Fig. 1 of the present application).

Clark et al. do not teach a polynucleotide sequence encoding SEQ ID NO:7, or 10 or 60 amino acid portions thereof, as recited in claims 3-5, as amended, and those claims dependent therefrom. Clark et al. also do not teach a 55 kDa antigen derived from an *I. multifiliis* G5 isolate.

It is clear from Fig. 3(a) of the present application, for example, that the 55 kDa i-antigen from a G5 isolate of *Ichthyophthirius*, which is the basis of the elected invention, is a different polypeptide from the 48 kDa i-antigen of Clark et al., with a different amino acid sequence. The 48 kDa i-antigen and the 55 kDa i-antigen are each encoded by different polynucleotide sequences. See p. 29, lines 25-31 of the specification. The 48 kDa i-antigen taught in Clark et al. and SEQ ID NO:7 do not have a length of at least 60 amino acids in common (claim 3), nor do they have terminal portions of 10 or more amino acids in common (claim 4).

Clark et al. therefore does not disclose each and every element as set forth in the claims 3-4, 6-10, 16 and 18. Reconsideration and withdrawal of the rejection of claims 3-4, 6-10, 16, and 18 under 35 U.S.C. §102(b) is respectfully requested.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claims 3-4, 6-10, 16, and 18 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed.

The Examiner states that the claims are vague and indefinite in the recitation of "polynucleotide fragment". Applicants disagree. However, solely to advance prosecution of the above-identified application, claim 3 is amended to recite a nucleotide sequence encoding an antigenic portion of an i-antigen polypeptide that comprises at least about 60 amino acids of

SEQ ID NO:7, and claim 4 is amended to recite a nucleotide sequence encoding a terminal portion of an i-antigen that comprise at least about 10 amino acids of SEQ ID NO:7.

The Examiner states that the claims are vague and indefinite in the recitation of "at least an antigenic portion" of an i-antigen. Applicants disagree. Antigenicity of an i-antigen is defined in detail at page 19, lines 16-23, of the specification for example. Solely to advance prosecution of the above-identified application, however, claim 3 is amended to delete the recitation of "at least" as being redundant and to recite that the antigenic portion of the i-antigen polypeptide is capable of inducing an immune response in a fish against *I. multifiliis*.

The Examiner states that claim 6 is indefinite in its recitation of an "organism." Applicants disagree. Nonetheless, in order to further prosecution claim 6 is amended to delete the recitation of an organism as being unnecessary, as the recitation of a cell without further limitation includes a cell within an organism. See also new claim 37 which depends from claim 6 and recites a cell that is part of a multicellular organism.

The Examiner states that the claims are vague and indefinite in the recitation of an antigenic polypeptide that shares a "significant level" of primary structure with another polypeptide. Applicants disagree, but in order to advance prosecution of the above-identified application have canceled claims 8 and 9.

The Examiner states that the claims are vague and indefinite in the recitation of "substantially complementary". Applicants disagree and direct the Examiner's attention to the specification at page 17, line 24 bridging to page 18, line 6, wherein the term "substantially complementary" is defined in detail to include certain hybridization activity and/or a certain level of nucleotide sequence identity.

The Examiner states that the claims are further vague and indefinite in recitation of "plurality of molecules", indicating that the number and identity of the molecules was not apparent. Applicants disagree; the term "plurality" is well-understood to mean two or more, and identity of the molecules (C3d component of complement) is clear.

In view of amendments to the claims and the arguments presented above, withdrawal of the rejection of claims 3-4, 6-10, 16, and 18 under 35 U.S.C. §112, second paragraph is respectfully requested.

Summary

It is respectfully submitted that the pending claims are in condition for allowance, and notice to that effect is earnestly solicited. The Examiner is invited to contact the Applicants' Representative at the below listed number if it is believed that prosecution of the above-identified application can be in any way assisted or expedited thereby.

Respectfully submitted,

Clark et al.

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APPENDIX A - PROPOSED CLAIM AMENDMENTS
INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 09/497,967
Docket No.: 235.00170101

Amendments to the following are indicated by underlining and shading what has been added and bracketing what has been deleted.

1. A nucleic acid molecule comprising a polynucleotide fragment having a nucleotide sequence that encodes at least a C-terminal portion of an i-antigen polypeptide having amino acid sequence SEQ ID NO:6.

2. The nucleic acid molecule of claim 1 comprising SEQ ID NO:1.

3. (Amended) A nucleic acid molecule comprising a polynucleotide fragment having a nucleotide sequence that encodes [at least] an antigenic portion of an i-antigen polypeptide having amino acid sequence SEQ ID NO:7, said antigenic portion of the i-antigen polypeptide comprising at least about 60 amino acids and being capable of inducing an immune response in a fish against *I. multifiliis*.

4. (Amended) A nucleic acid molecule comprising a polynucleotide fragment having a nucleotide sequence that encodes at least one terminal portion of an i-antigen polypeptide having amino acid sequence SEQ ID NO:7, said terminal portion comprising at least about 10 amino acids.

5. (Amended) [The] A nucleic acid molecule [of claim 4] comprising a polynucleotide fragment having a nucleic acid sequence that encodes SEQ ID NO:7 [SEQ ID NO:3 or SEQ ID NO:5].

6. (Amended) The nucleic acid molecule of any of claims [1, 3 or 4] 3-5 or 36 that is a vector capable of expressing the polypeptide encoded by the nucleic acid sequence in a

cell [or an organism, wherein the cell or organism is] selected from the group consisting of a bacterium, a protozoan, a yeast, an insect cell, and an animal cell [or organism].

7. The nucleic acid molecule of claim 6 that is capable of expressing the polypeptide encoded by the nucleic acid sequence in *E. coli*, *Pischia pastoris* or *Tetrahymena*.

8. (Cancelled)

9. (Cancelled)

10. (Amended)A nucleic acid molecule that is substantially complementary to any of the nucleic acid molecules of claims [1, 3, 4, or 8] 3-5 or 36.

11. (Amended) A nucleic acid molecule comprising a polynucleotide fragment that hybridizes to at least a portion of the complement of [at least one of SEQ ID NO:1 or] SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:44 or SEQ ID NO:102 under standard hybridization conditions, wherein the polynucleotide fragment encodes a polypeptide comprising at least a membrane targeting portion or an antigenic portion of an i-antigen protein, wherein said antigenic portion is capable of inducing an immune response in a fish.

12. The transgenic *T. thermophila* of claim 11 wherein the portion of the *I. multifiliis* i-antigen protein comprises a targeting amino acid sequence.

13. The transgenic *T. thermophila* of claim 12 wherein the targeting amino acid sequence comprises at least one of an N-terminal targeting sequence and a GPI cleavage/attachment sequence.

14. (Amended) A composition for inducing an immune response in a fish, said composition comprising at least one [component selected from the group consisting of (a) a polypeptide comprising an antigenic portion of an i-antigen polypeptide and (b) a] nucleic acid molecule [comprising a polynucleotide fragment having a nucleotide sequence encoding an antigenic portion of an i-antigen polypeptide] of any of claims 3-7, 10, 11 or 36.

15. The composition of claim 14 comprising a polypeptide of claim 13.

16. (Cancelled)

17. The composition of claim 14 wherein administration of the composition to fish prevents or controls *I. multifiliis* infection.

18. (Amended) The composition of claim 14 [comprising a nucleic acid molecule comprising a polynucleotide fragment having a] wherein the nucleotide sequence [encoding] encodes an antigenic portion of an i-antigen polypeptide linked at its carboxy-terminus to a plurality of molecules of the C3d component of complement.

19. The composition of claim 14 formulated for oral administration.

20. The composition of claim 19 wherein the polypeptide or nucleic acid molecule is encapsulated in a biodegradable polymer.

21. A host cell transformed with the nucleic acid molecule of claim 6.

22. The method of claim 20 wherein the antigenic polypeptide is a pathogenic parasite polypeptide, and wherein the host cell is exposed to the bodily fluid of a patient suspected of being infected with the parasite.

23. (Amended) Transformed *Tetrahymena* comprising the nucleic acid molecule of any of claims [1, 3 or 4] 3-11 or 36.

24. An antibody capable of binding a polypeptide of claim 12.

25. A method for detecting *Ichthyophthirius* in an aquaculture comprising:
obtaining a sample containing nucleic acid from an aquaculture fish or an aquaculture water;
adding at least one primer oligonucleotide having a sequence complementary to at least a portion of SEQ ID NO:1 or SEQ ID NO:3 to the nucleic acid sample;
conducting a polymerase chain reaction amplification with the sample;
and analyzing the reaction mixture for the presence of a product amplified by the at least one oligonucleotide primer.

26. The method of claim 25 wherein the primer is capable of amplifying nucleotide sequences encoding i-antigens derived from least two different *I. multifiliis* serotypes.

27. The method of claim 26 wherein the primer has a nucleic acid sequence that encodes an amino acid sequence selected from the group consisting of MKYNILLT (SEQ ID NO:36), FLSISLLF (SEQ ID NO:38), GTALDDGV (SEQ ID NO:46), AGTDTCT (SEQ ID NO:48), CTKKLTSGA (SEQ ID NO:50) and FAKFLSISL (SEQ ID NO:52).

28. The method of claim 25 further comprising making an polynucleotide vaccine comprising at least a portion of the amplified product, wherein the portion of the amplified product encodes an antigenic polypeptide.

29. The method of claim 25 further comprising making a protein subunit vaccine comprising an antigenic polypeptide encoded by at least a portion of the amplified product.

30. The method of claims 28 or 29 further comprising administering the vaccine to fish to treat or prevent *Ichthyophthirius* infection.

31. A method for identifying an *I. multifiliis* serotype comprising:
providing a sample comprising an *I. multifiliis* nucleic acid molecule having a nucleotide sequence encoding an i-antigen;
adding to the sample at least one primer oligonucleotide having a sequence complementary to a unique region of an *I. multifiliis* nucleotide sequence encoding an i-antigen;
subjecting the sample to amplification conditions; and
analyzing the sample to determine the presence of a product amplified by the at least one oligonucleotide primer.

32. A method for inducing an immune response in a fish comprising administering to the fish the immunogenic composition of claim 14.

33. The method of claim 32 performed prophylactically in advance of exposure to *I. multifiliis*.

34. The method of claim 32 performed therapeutically while the fish is infected with *I. multifiliis*.

35. The method of claim 32 wherein administration is performed by injection, immersion, or oral ingestion.

36. (New) The nucleic acid molecule of claim 5 comprising at least one nucleotide sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:44 and SEQ ID NO:102.

37. (New) The nucleic acid molecule of claim 6 wherein the cell is part of a multicellular organism.